Tissue free DNA precipitates hydroxyl-apatite crystals in the arterial wall.

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Arterial wall calcium score, quantified by X-ray scanning, is now used in clinical practice as one of the strongest biomarkers of cardiovascular risk. Calcium phosphate and hydroxyapatite retention in the arterial wall necessitate precipitation on a tissue anionic platform. In the present study we explore the potential role of tissue free DNA as one of this platform. For this purpose we developed both an observational approach on human early stages of atheroma and an experimental demonstration by infusing free DNA in the arterial wall of rats.

The first step consisted in histological examination of samples from human and rat spontaneously calcified arteries. Various stains were used to evaluate co-localization of free DNA with calcified tissues before and after section treatment by EDTA.In a second step, a rat model of vascular calcifications provoked by various intra-aortic infusions of free DNA and free DNA + elastase was assessed. Rats underwent a micro-CT for calcium score calculation before being sacrificed at 3 weeks.

Our histological study shows a co-localization of calcified arterial plaques with free DNA in human atherosclerotic lesions and in the wall of aneurysm in rats. In the intra-aortic infusion model, free fragmented DNA was able to cross the arterial wall and induce calcifications whereas no microscopic calcification was seen in sham aortas. The calcification score of the free DNA + elastase was significantly higher than the free DNA group (p =.02) and the control group (p <.001). Qualitative evaluation with Fourier Transform Infrared Spectroscopy (FTIR) and Scanning Electron Microsopy (SEM) demonstrated typical hydroxyapatite crystal retention in calcified human and rat aortas, and calcium phosphate precipitation in human specimens.

This translational study demonstrates that tissue free DNA can precipitate hydroxyl-apatite crystals forming calcifications in the arterial wall.